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20231

PATENT  
Attorney Docket No.: 017473-001110US

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4-16-01  
Done

On April 6, 2001

TOWNSEND and TOWNSEND and CREW LLP

By: Annette S. Parent

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Glenna C. Burner, *et al.*

Application No.: 09/292,758

Filed: April 14, 1999

For: NUCLEIC ACID SEQUENCES  
AND PROTEINS ASSOCIATED WITH  
AGING

Examiner: B. Sisson

Art Unit: 1655

AMENDMENT

Art Unit 1655  
Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

In response to the Office Action mailed December 6, 2000, Applicants respectfully request reconsideration in view of the following remarks and amendments. A petition to extend the time for response for one month, from March 6, 2001 to April 6, 2001, is submitted herewith. Please amend the above-identified application as follows:

IN THE CLAIMS: ✓

Please amend claims 7, 29, 38, 55, and 62 as follows.

Please cancel claim 30 without prejudice to subsequent revival.

7. (once amended) An isolated nucleic acid comprising a polynucleotide sequence associated with the senescence of a cell, wherein said polynucleotide sequence

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B<sup>1</sup>  
concl'd

hybridizes to a nucleic acid having a sequence as set forth in SEQ. ID. NO:1 under stringent conditions, which comprise hybridization in a solution comprising 50% formamide at 42°C and washing in a solution comprising 0.2x SSC wash at 65°C.

subF4  
B<sup>2</sup>

29. (once amended) A kit for detecting whether a cell is undergoing senescence, said kit comprising:  
a probe which comprises a polynucleotide sequence selected from the group consisting of SEQ ID NO:1, 2, 38, 55, 61, 67, 69, 70, and 73; and  
a label for detecting the presence of said probe.

B<sup>3</sup>

38. (once amended) A kit for detecting whether a cell is G0-arrested, said kit comprising:  
a probe which comprises a polynucleotide sequence selected from the group consisting of SEQ ID NO:1, 2, 38, 55, 61, 67, 69, 70, and 73; and  
a label for detecting the presence of said probe.

B<sup>4</sup>

55. (once amended) A kit for detecting whether a fibroblast cell is aging, said kit comprising:  
a probe which comprises a polynucleotide sequence selected from the group consisting of SEQ ID NO:1, 2, 38, 55, 61, 67, 69, 70, and 73; and  
a label for detecting the presence of said probe.

B<sup>5</sup>

62. (once amended) A kit for detecting whether a skin cell is aging, said kit comprising:  
a probe which comprises a polynucleotide sequence selected from the group consisting of SEQ ID NO:1, 2, 38, 55, 61, 67, 69, 70, and 73; and  
a label for detecting the presence of said probe.

### REMARKS

With this amendment, claims 1-3, 6-11, 29, 31-33, 38, 39, 55, and 62 are pending in the present application and under examination. Claims 7, 29, 38, 55, and 62 are amended. Claim 30 is canceled. Claims 4, 5, 12-28, 34-37, 40-54, 56-61, and 63-72 were withdrawn from consideration as drawn to a non-elected invention, and have been canceled without prejudice to subsequent revival. Appendix A provides the version with markings to show change to the amended and new claims. Appendix B shows all pending claims currently under examination.

#### ***Status of the claims***

Claims 29, 38, 55, and 62 were amended to recite a polynucleotide sequence "selected from the group consisting of SEQ ID NO:1, 2, 38, 55, 61, 67, 69, 70, and 73." This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on pages 61-65.

#### ***Objection to claim 30***

Claim 30 was objected to as it recites SEQ ID NOS: that are drawn to non-elected inventions. Claim 30 has been canceled, so the objection is moot.

#### ***Rejection under 35 U.S.C. § 112, first paragraph: written description***

Claims 1-3, 6-11, 13, 14, 29-33, 38, 39, 55, 56, 62, and 63 were rejected as allegedly containing subject matter that was not described in the specification as originally filed. In the Office Action, the Examiner observed that the purpose of the written description requirement is to convey to one of skill in the art that the inventor was in possession of the invention as of the filing date. The rejection then stated that "[w]hile some of the claims place limits on the percent variability of the various nucleic acid sequences, the specification has not been found to provide an adequate written description of same to the extent that it reasonable conveys that applicants was in possession of such innumerable variants." Office Action, page 3.

Applicants first note that claims 29, 31, 38, 55, and 62 have been amended to recite a sequence selected from the group consisting of "SEQ ID NO:1, 2, 38, 55, 61, 67, 69, 70, and 73." These claims therefore now recite the sequences that the Examiner indicated met the written description requirement. To the extent that the rejection applies to the claims as amended, Applicants respectfully traverse.

The claims fully comply with the requirements for written description as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The claims set forth structural elements based on reference nucleic acid or amino acid sequences, e.g., either (1) reference amino acid sequences against which antibodies are raised, which specifically bind to the claimed sequences; (2) reference nucleic acid sequences to which the claimed sequences have a specified percent identity; and (3) reference nucleic acid sequences to which the claimed nucleic acids hybridize under specified hybridization conditions. Therefore, the claimed sequences are thereby defined via shared physical and structural properties.

As described above, the present invention relates to the discovery of nucleic acids and proteins associated with the aging process. The senescence-associated nucleic acids and the proteins that they encode are claimed by reference to shared structural features, i.e., nucleic acid and amino acid sequences. As described above, the claims provide sequences that bind to antibodies raised against the reference sequences, hybridize to the reference sequences, or have a specified identity to the reference sequences.

The ability of a particular nucleic acid to hybridize under *given conditions* to a reference nucleic acid is a physical/structural property of the nucleic acid, because it relies upon the nucleotide sequence of the molecule (*see, e.g.,* Sambrook, *Molecular Cloning: A Laboratory Manual*, pp. 9.47-9.51 (2nd ed. 1989); *see also* Stryer, *Biochemistry*, pp. 573 (2nd

ed. 1975)). As described in Stryer, the transition between hybridization and melting of complementary nucleic acid strands is abrupt and largely sequence dependent. When the temperature of hybridization is provided, one of skill in the art would be able to predict whether or not a given sequence would hybridize to a reference sequence (*see, e.g.*, equations provided in Sambrook, *supra*). Moreover, in the same light, the percent identity of a nucleic acid to a reference sequence is a structural feature, as it relies entirely on the sequence of the molecule. Furthermore, the ability of an antibody to specifically bind to an amino acid sequence is a structural feature, as it relies entirely on the sequence of the molecule.

In the present application, Applicants have provided both reference nucleotide and amino acid sequences, as well as hybridization conditions and sequence analysis algorithms. As required by the standard set forth in *University of California v. Eli Lilly*, these structural features are common to all of the members of the claimed nucleic acids and the proteins they encode. The conserved sequences encoding these structural features, and the given conditions under which the claimed sequences would hybridize to such reference sequences or have a specified identity to such sequences or bind to antibodies raised against such sequences "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*see*, Office Action, page 4, *quoting Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 111, 1116 (Fed. Cir. 1991)). The specification thus appropriately describes the claimed senescence associated nucleic acid and protein genus using structural/physical features, as required by the court in *University of California v. Eli Lilly*. As such, Applicants respectfully request that the Examiner withdraw the rejection.

***Rejection under 35 U.S.C. § 112, second paragraph***

**"Stringent conditions"**

Claim 7 was rejected as allegedly indefinite with respect to what constitutes stringent conditions. Claim 7 has been amended to recite specific stringent conditions. Applicants therefore respectfully request that the rejection be withdrawn.

"Associated"

Claims 29 and 55 were rejected as allegedly indefinite for reciting the term "associated." Claims 29 and 55 have been amended to delete this term. Applicants respectfully request that the rejection be withdrawn.

***Rejection under 35 U.S.C. § 102/103***

Claims 29-33, 38, 39, 55, and 62 were rejected as allegedly anticipated and/or obvious over Brennan. Brennan discloses a nucleotide array that comprises every possible oligonucleotide of 10 residues in length. The rejection contends that by default, such an array would comprise sequences that are specific for Applicants sequences. Office Action, page 6.

Applicants first note that claims 29, 31, 38, 55, and 62 have been amended to recite polynucleotide probes "selected from the group consisting of SEQ ID NO:1, 2, 38, 55, 61, 67, 69, 70, and 73."

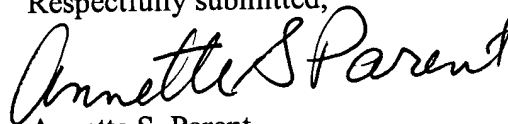
To the extent that the rejection applies to the claims as amended, Applicants respectfully traverse. "For a prior art reference to anticipate in terms of 35 U.S.C. §102, every element of the claimed invention must be identically shown in a single reference." *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). However, the claimed invention is a selection invention, which claims only specified probes from polynucleotides associated with cellular senescence and aging. The genus of all possible 10-mer oligonucleotide probes of Brennan therefore fails to teach the specific collection of probes claimed by Applicants. Instead, Brennan teaches random 10-mers that encompass "every possible oligonucleotide of 10 residues in length." The claimed reference therefore fails to either teach or suggest the specific collection of claimed nucleic acids. Applicants respectfully suggest that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

A handwritten signature in cursive script that reads "Annette S. Parent".

Annette S. Parent  
Reg. No. 42,058

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, 8<sup>th</sup> Floor  
San Francisco, California 94111-3834  
Tel: (415) 576-0200  
Fax: (415) 576-0300  
SF 1210419 v1